

The cost of hospital care and pharmaceuticals 2009 – 2012 for patients with rheumatoid arthritis in Norway.

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Master Thesis

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Andreas Eriksen
Oslo, May 2014

SUMMARY

Rheumatoid arthritis is an inflammatory disease that affect 0.5% - 1.0% of the population world-wide and approximately 0.5% in Norway. RA places a considerable burden on patients in terms morbidity and mortality, and on society in terms of costs.

The aim of this master thesis was to explore the costs of hospital care and pharmaceuticals in patients with rheumatoid arthritis and study the differences in these costs across time and region.

Data on all episodes of hospital care during 2009 – 2012 were collected from the Norwegian Patient Registry using «M05 – Seropositive rheumatoid Arthritis» and «M06 – Other Rheumatoid Arthritis» as either main or secondary diagnoses as inclusion criteria. The data included information about age-group, sex, region, diagnosis and use of biologic pharmaceuticals. Data on pharmaceuticals dispensed from pharmacies during 2009 – 2012 were extracted from the Norwegian Prescription Database.

The estimated total costs of hospital care and pharmaceuticals for rheumatoid arthritis in Norway were NOK1 billion in 2012. Hospital care and biologic DMARDs administered in hospital accounted for 58%, private specialist care 0.6%, rehabilitation in private clinics 1.0% and prescription drugs 40% of the costs. The registered hospital care costs increased during 2009-2011 and decreased by 5% from 2011 to 2012. Per capita hospital care costs varied considerably with a difference of more than 20% between the regional health authority with the lowest and the highest costs. The costs of private specialist care were considerably higher in the South-Eastern- and the Western Norway regional health authority compared to the Northern- and the Central Norway regional health authority in terms of total costs and costs per capita. The costs of care in private rehabilitation clinics decreased during the period and differed across regions. The Northern Norway regional health authority had the highest- and the Western Norway regional health authority had the lowest costs of care in private rehabilitation clinics. The costs of patient-administered disease modifying antirheumatic drugs (DMARDs) (Biologic and non-biologic) increased from NOK351 million to NOK414 million during the period. Despite the increasing use of DMARDs there was no reduction in rheumatic surgery.

ABBREVIATIONS

| | | |
|-------|---|---|
| ACR | - | American College of Rheumatology |
| CBA | - | Cost Benefit Analysis |
| CCA | - | Cost Consequence Analysis |
| CEA | - | Cost effectiveness Analysis |
| CMA | - | Cost Minimization Analysis |
| COI | - | Cost of Illness |
| CUA | - | Cost Utility Analysis |
| DALY | - | Disability Adjusted Life Year |
| DMARD | - | Disease-modifying antirheumatic drug |
| EULAR | - | European League Against Rheumatism |
| GP | - | General Practitioner |
| HCA | - | Human Capital Approach |
| HRQoL | - | Health Related Quality of Life |
| ICER | - | Incremental Cost Effectiveness Ratio |
| IMR | - | Incidence Mortality Rate |
| NOK | - | Norwegian Crowns (The Norwegian currency) |
| NPR | - | Norwegian Patient Registry |
| NSAID | - | Analgesics and non-steroidal anti-inflammatory drug |
| QALY | - | Quality Adjusted Life Year |
| QoL | - | Quality of Life |
| RA | - | Rheumatoid Arthritis |
| RCT | - | Randomized Controlled Trial |
| RHA | - | Regional Health Authority |
| SMR | - | Standardized Mortality Rate |
| SSB | - | Statistics Norway |
| WHO | - | World Health Organization |

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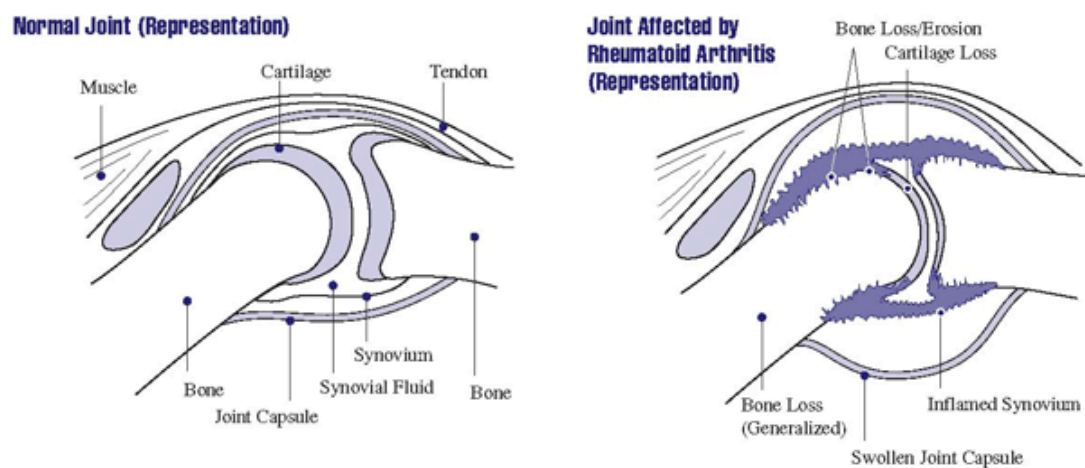
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1. Background

1.1 Pathology

Rheumatoid arthritis (RA) is an inflammatory disease that causes pain, swelling, stiffness and loss of function in the joints. It occurs when the immune system, which normally defends the body from invading organisms, turns its attack against the membrane lining the joints. (1) It is an autoimmune disorder causing symmetrical polyarthritis of large and small joints, typically presenting between the ages of 30 and 50 years (2) Figure 1 illustrates a healthy joint and a joint that is affected by RA.

FIGURE 1 Illustration of a normal joint and a joint affected by RA



Source: NIH: National Institute of Arthritis and Musculoskeletal and Skin Diseases

It is not known what triggers the onset of RA. Many have tried to identify factors that increase the probability of developing of the disease. Genetics (3), environmental factors and infectious agents (4, 5) have all been suggested as possible risk factors. Moreover, several lifestyle features are seen among RA-patients, and of the most important is smoking status. Di Guiseppe and co-workers (6) conclude that smoking is positively associated with Rheumatoid arthritis in their meta-analysis of studies on smoking and RA.

1.2 HRQOL in rheumatoid arthritis

Quality of life (QoL) is the perceived level of happiness or gratification in life, or the individual's perception of its situation within a given system of culture and values.

Rheumatoid arthritis is among the main conditions where QoL is decreased (7).

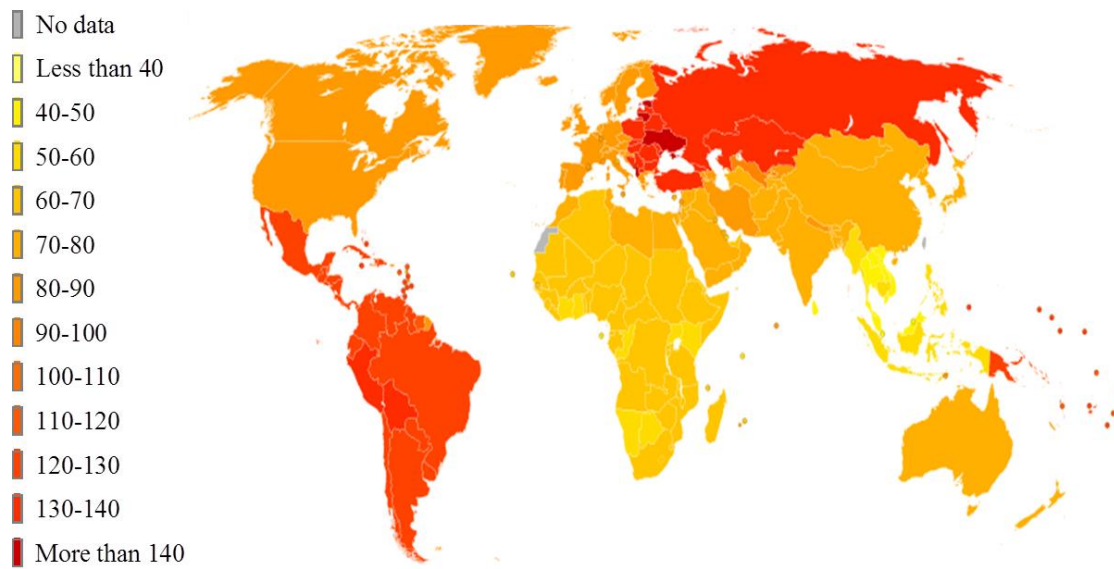
Health related quality of life (HRQoL) is an assessment of the effect a disease, disorder or disability has on a person's well-being. The severely debilitating nature of rheumatoid arthritis causes challenges in the day to day life of people who develop the disease. RA leads to physical activity limitation, disability and premature death.

Patients with RA who have significant functional disability have three times higher risk of mortality compared to the general population (8). Other complications associated with the disease are reduced social functioning and a worsening of mental health. Health related quality of life in patients with RA is often affected by disability, pain, fatigue, depression and comorbidities (9). Rheumatoid arthritis is usually viewed as having substantial effect on all aspects of HRQoL (10). Ouyalu and co-workers (11) found that RA has a negative impact on HRQoL and that RA-patients scored lower than healthy individuals on both the mental - and the physical component.

1.3 Epidemiology

Rheumatoid arthritis affects 0.5% - 1.0% of the population in developed countries (12), and approximately 0.5% in Norway (13). The illness is three times more frequent in women than men and prevalence increases with age. Incidence ranges from 5 to 50 per 100 000 in the adult population in developed countries (12), and approximately 25 per 100,000 in Norway (14, 15). Several studies show a decline in RA incidence the last decades (16-18). Figure 2 shows the global burden of rheumatoid arthritis. The figure is based on data from WHO's DALY estimates from 2004.

FIGURE 2 Age-standardized disability-adjusted life year (DALY) rates from Rheumatoid arthritis by country (per 100,000 inhabitants) 2004.



Source: Vector map from BlankMap-World6, compact.svg by Canuckguy et al., Data from Death and DALY estimates for 2004 by cause for WHO Member States (Persons, all ages) (2009-11-12). WHO

URL: http://commons.wikimedia.org/wiki/File:Rheumatoid_arthritis_world_map_-_DALY_-_WHO2004.sv

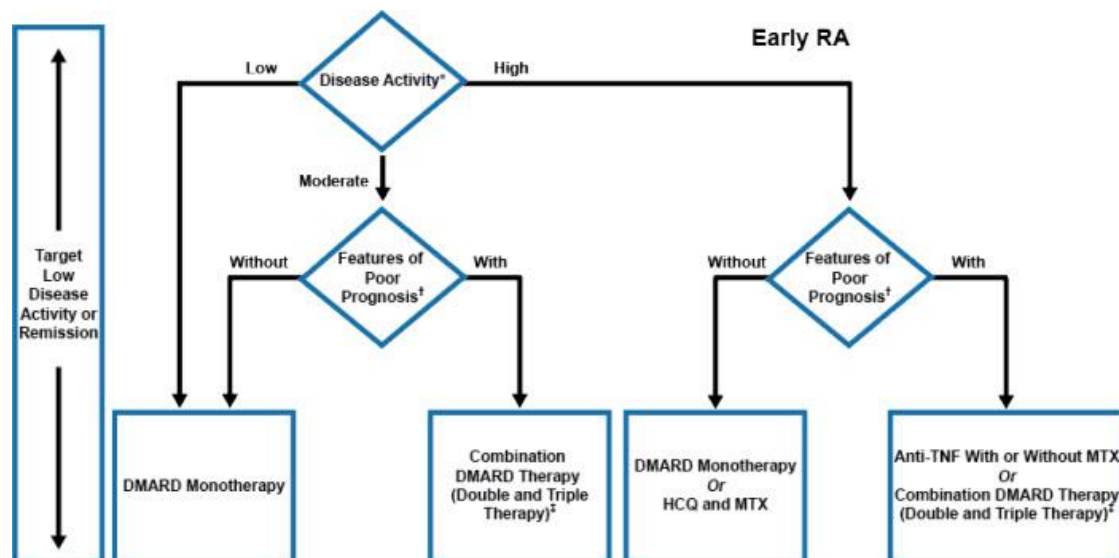
The main causes of death among rheumatoid arthritis-patients are increased incidence of cardiovascular disease, respiratory diseases, cancer and infections (19-22). Dadoun and co-workers (23) performed a systematic review of studies on mortality in RA the last fifty years and found that mortality has decreased among RA-patients, but remains higher than for the general population. The review revealed a decrease in the incidence mortality rate¹ (IMR) from 4.7/100 patient-years before 1970 to 2/100 patient-years after 1983. IMR is here a measure of the mortality among the RA population. Mean IMR was measured at 2.7/100 patient-years. They did not, however, find a significant decrease in standardized mortality rate (SMR: the ratio of deaths in the RA population to the expected deaths in the general population). 8 studies in the review reported SMR (21, 22, 24-29) varying from 0,87 to 2,03. Only one study reported SMR < 1 while the other seven studies reported SMR > 1, indicating a higher mortality rate among RA-patients compared to the general population.

¹ Incidence mortality rate = Number of deaths at the end of the study / (mean number of patient during study * mean patient follow up)

1.4 Treatment

Several national and regional guidelines for management of rheumatoid arthritis exist, including recommendations from The American College of Rheumatology (ACR) (30) and the European League against Rheumatism (EULAR) (31). The management of rheumatoid arthritis rests on several principles. A comprehensive approach to RA-treatment consists of patient education, physical/occupational therapy and drug treatment (31, 32). RCTs have shown positive effect on muscle strength and quality of life from physical exercise in RA-patients (33, 34). Moreover, ACR stress the importance of patient education and claim it is critical to engage the patient in an effective partnership for managing the disease (30). Analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to control RA symptoms. They do not, however, alter the progression of the disease. Analgesics reduce pain and NSAIDs reduce pain and stiffness. Disease-modifying antirheumatic drugs (DMARDs) are the mainstay in the treatment of RA-patients. EULAR recommends starting treatment with synthetic DMARDs early and that this may help a significant proportion of patients to achieve low disease activity or remission. (31) ACR also state the importance of introducing DMARDs in early stages of RA-treatment in their *"2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of RA"*(35) (Figure 3). Biologic DMARDs were introduced in the late 1990s and are the latest major addition to RA treatment. DMARD-treatment has undergone dramatic changes during the last decades, yielding a new therapeutic dimension to RA-treatment (31). DMARDs have been found to reduce symptoms such as joint swelling and pain. Moreover, they decrease acute-phase markers, limit progressive joint damage, and improve patient`s general functionality (12).

FIGURE 3 Treatment with DMARDs in early RA



DMARD = disease-modifying antirheumatic drug; HCQ = hydroxychloroquine; MTX = methotrexate; RA = rheumatoid arthritis; TNF = tumor necrosis factor.

† Patients were categorized based on the presence or absence of 1 or more of the following poor prognostic features: functional limitation (eg, Health Assessment Questionnaire score or similar valid tools), extraarticular disease (eg, presence of rheumatoid nodules, RA vasculitis, Felty's syndrome), positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, and bony erosions by radiograph.

‡ Combination DMARD therapy with 2 DMARDs, which is most commonly MTX based, with some exceptions (eg, MTX + HCQ, MTX + LEF, MTX + sulfasalazine, and sulfasalazine + HCQ), and triple therapy (MTX + HCQ + sulfasalazine).

Singh JA, et al.(35)

1.5 Cost

Costing has three basic elements: Identifying cost variables, measurement of the quantities of the resource use and assigning a unit price to each cost variable (36). Our study is limited to hospital care costs and costs of pharmaceuticals. An analysis of total societal cost of a disease involves measuring both direct and indirect cost. Direct cost can be divided in two categories: direct medical cost and direct nonmedical cost. Direct medical cost includes pharmaceuticals, GP-visits, in-hospital care, out-hospital care, rehabilitation and other cost variables that are directly connected to medical treatment. Direct nonmedical cost includes travel expenses, home assistance costs and other direct cost variables that are not of a medical nature. Indirect cost is often limited to production losses and production gains. The method in which to estimate production costs remains a much debated topic in the field of economic evaluation. Guidelines from Sweden recommend that production costs are estimated using the

Human Capital Approach (HCA), which values production costs based on gross earnings. Some argue that HCA leads to an overestimation of the true cost and argue that production costs should be estimated using the friction cost method (37, 38). The reasoning is that if an individual is taken out of the workforce, losses in production will be compensated for, to some degree, by collages or, in the case of long time sick leave, by hiring a replacement worker. And that ultimately, someone unemployed will enter the workforce leading to production gains (36). The basic idea of the friction cost method is that the amount of production loss due to sick leave is limited to the time span the organisation needs to restore the initial production level (36, 37). According to Drummond (36) the actual cost of any resource use is not the amount of money spent, but rather the opportunity cost, defined as the value of the foregone benefits that may have been achieved had the resource been available for its best alternative use. In lack of opportunity cost we have used Norwegian DRG prices for estimating in-hospital care costs and market prices for estimating the cost of pharmaceuticals. Data on quantities of resource use related to in-hospital care and pharmaceuticals are collected from the Norwegian Patient Registry and the Norwegian Prescription Database respectively.

1.6 Economic evaluation

Scarce resources and the development of new and costly treatment are the main drivers of health economics. This and a general rise in awareness among policymakers of the importance of theoretical foundation of priority decisions have led to an increase in the demand for economic analyses in medicine.

A Cost of Illness analysis (COI) is one of many in the wide range of cost analyses. Other common cost analyses include Cost Utility Analysis (CUA), Cost Effectiveness Analysis (CEA), Cost Minimization Analysis (CMA), Cost Benefit Analysis (CBA) and Cost Consequence Analysis (CCA).

CMA compares the cost of interventions that produce identical effect. CBA examines the total costs and benefits in monetary terms. CCA lists the cost variables and their

consequences separately to allow the end user to focus on the variables that are relevant in their case (39).

In medicine, most economical research has taken the form of CUA or CEA. CEA is designed to assess the comparative effects and expenditures of two or more health interventions. This involves estimating the incremental cost and effect of an intervention compared to an alternative- or no intervention (40). The importance of CEA is the assessment of the relative impact of these interventions on health in environments with limited resources. A useful result of a CEA is the Incremental Cost Effectiveness Ratio (ICER) which expresses the additional cost required to obtain one unit of health effect from a given intervention when compared to another (41). When the intervention under study is both less costly and more effective than the comparator, the intervention dominates the alternative and there is no need for the ICER. However, the most common case is one where the new intervention is both more effective and more costly than its alternative. Interventions with a low ICER would then have high priority for resources (40). Hence, CEA and the ICER are useful to decision makers for priority setting. CUA is similar to CEA in many ways and share the characteristics described above, but where CEA measures effect in program specific natural units related to the program, CUA measures effect in Quality Adjusted Life Years (QALYs) or other generic units. This quality of the CUA allows for comparison across a broad set of interventions (36).

1.7 Cost of Illness

A COI – analysis measures the economic burden of a disease and estimate the maximum amount that could potentially be saved or gained if a disease were to be eradicated. (42) There are two main approaches to COI analysis. The prevalence- and the incidence approach. A prevalence based analysis includes all costs incurred in a given year and yield accurate costs based on observed data. The prevalence approach yields a measure of total annual costs. With an incidence approach, the analysis is based on all new episodes in a given year and all costs related to the new episodes are measured. Additionally, all future costs are estimated for the same patient group and converted to the present value and added to the cost incurred in the index year. The

advantage of the latter approach is that it provides projections of future costs. Such projections, however, may be uncertain (43). COI can identify where the major burden of cost might lie in the treatment and care of patients with a certain disease (44). COI may also be useful in funding of health care services and setting priority for research (43). Moreover, COI studies provide valuable information for cost-effectiveness and cost-benefit analyses. There are, however, limitations to the use of COI studies. COI does not include any measurement of health effects of the disease. Nor does it include the benefits from treatment. Unlike CEA, COI does not aim to inform choices on which treatment program is more cost effective. Hence, it cannot, in itself, justify allocation of resources in priority decisions (43, 44).

1.8 Literature review of RA cost studies

In order to get an overview of studies on costs of rheumatoid arthritis, we performed a search (2013.10) in the Medline database using the following search terms in title and abstract:

- Rheumatoid arthritis
- RA
- Cost
- Burden of illness
- Burden of disease

The search was built to include articles that contain “Rheumatoid arthritis” or “RA” and at least one of the other 3 keywords and was limited to the time interval 01.01.2003 – 31.12.2013. The search generated 994 hits of which 6 (42, 45-49) were considered relevant based on the following inclusion criteria:

- The study is conducted in Europe or North America.
- The study is conducted in the time period: 2000 – 2013.
- The study includes direct cost of RA.
- The article is written in English.
- The study includes estimates on hospital cost and cost of pharmaceuticals

A summary of the studies and results is presented in table 1. Currency conversion is based on annual average exchange rates from the Norwegian National Bank². The present value of historic costs is calculated using actual inflation rates extracted from Statistics Norway's online database³.

TABLE 1 Studies of cost in rheumatoid arthritis 2003 - 2013

| Author | Published | Year of data collection | Study area | Direct cost ^a | Hospital care costs ^a | Pharmaceutical costs ^a |
|--------------------|-----------|-------------------------|------------|--------------------------|----------------------------------|-----------------------------------|
| Guillemin et al. | 2004 | 2000 | France | 41 398 | 25 130 | 5 171 |
| Westhovens et al.* | 2005 | 2000 | Belgium | 68 723 | 5 975 | 8 960 |
| Franke et al.*** | 2009 | | Europe | 58 443 | | |
| Huscher et al. | 2006 | 2002 | Germany | 42 895 | 20 356 | 16 381 |
| Jacobsson et al. | 2007 | 2001 | Sweden | 47 333 | 12 357 | 21 645 |
| Kvamme et al.** | 2012 | 2000-2012 | Norway | 51 011 | 18 630 | 19 122 |
| Average | | | | 51 634 | 16 490 | 17 820 |

^a Mean annual cost in 2012 NOK

* An average of early and late rheumatoid arthritis

** Weighted average of patients on synthetic and biologic DMARDs

*** A systematic review

Despite the similarities in economic status between the countries in this literature review, it is likely that there are differences in resource use and price levels. Hence, comparing costs must be done with caution.

The latest Norwegian study on the cost of Rheumatoid Arthritis was performed by Kvamme and co-workers. (48). The main objective of their study was to estimate the total cost for patients with rheumatoid arthritis, ankylosing spondylitis and psoriasis

² <http://www.norges-bank.no/no/prisstabilitet/valutakurser>

³ <https://www.ssb.no/statistikkbanken/selectvarval/Define.asp?subjectcode=&ProductId=&MainTable=KpiAar&nvl=&PLanguage=0&nyTmpVar=true&CMSSubjectArea=priser-og-prisindekser&KortNavnWeb=kpi&StatVariant=&checked=true>

arthritis. Their main data source was the Norwegian DMARD register (NOR DMARD) which records resource use among patients starting therapy with synthetic and biologic DMARDs. The total annual costs per patient of RA were estimated to € 36,826 in 2010 EUROS or 313,119 in 2012 Norwegian Kroner (NOK). Using the human capital method to calculate the production loss, production losses were the largest cost component followed by the cost of biologic DMARDs and the cost of in-hospital treatment. When the friction cost method was used, biologic DMARDs represented the largest cost component followed by production loss. Direct costs were estimated at NOK51,011 per patient, of which NOK18,630 was attributable to hospital care and NOK19,122 pharmaceuticals. The study covered the two first years of treatment. The authors found that the costs were declining during this period, hence, the total annual cost estimates in this study may be higher than the average annual costs of RA-patients. Moreover, all patients in the NOR-DMARD registry are treated with DMARDs, thus, the cost of pharmaceuticals in this study is likely to be higher than for the average RA-patient.

Jacobssen and co-workers (47) surveyed a representative sample (n=895) patients living in the city of Malmo, Sweden, during 2002. The objective of the study was to estimate the cost of living with RA. The authors estimated the mean annual direct cost to 44,485 Swedish kroner (SEK) or NOK47,333 (in 2012 NOK). Annual hospital costs were estimated to NOK12,357 per patient and annual cost of pharmaceuticals were estimated to NOK21,645 per patient. The authors state that their estimates are higher than earlier studies and suggest that the reason may be that they have a bottom up perspective, yielding more cost variables. The authors also point to the increase in medication cost compared to earlier studies and state that costs have increased from 4% to 18.8% of total cost compared to similar studies in Sweden in the 1980s and 1990s and that the main explanation is the introduction of TNF-inhibitors in the treatment of RA-patients.

Huscher and co-workers (42) estimated the direct and indirect cost of rheumatoid arthritis in Germany. They used the National Database of the German Collaborative Arthritis Centres to compute the cost and found that mean direct cost amounted to NOK42,895 and that of this, NOK20,356 was attributable to hospital care and

NOK16,381 to pharmaceuticals. The authors state that their findings are in line with those of other cost of illness-studies and that their estimates underline the high economic burden of RA.

Guillemin and co-workers (46) performed a cost of illness study of rheumatoid arthritis-patients in France. They collected data through a cross sectional study among rheumatologists in 148 hospitals and found that social cost represented 41% of total cost and that direct cost represented 59%. Annual direct cost per patient amounted to NOK41,398 of which 60 % or NOK25,130 was attributable to hospitalization. Annual cost of pharmaceuticals were reported at NOK5,171 per patient, however, this estimate does not take in to account the cost of TNF-inhibitors that were introduced in France at the time. This might explain why the cost estimate for pharmaceuticals in this study is significantly lower than that of the other studies in the review.

Additionally, in 2013, Lærum and co-workers produced a comprehensive report on the musculoskeletal diseases in Norway in terms of prevalence and societal costs.(50) This report, however, only present aggregated costs estimates.

2. Objective

The overarching aim of this thesis was to estimate the cost of pharmaceuticals and hospital care among patients with rheumatoid arthritis in Norway. More specifically we aim to explore the following research questions:

- What are the total costs of pharmaceuticals and hospital care of rheumatoid arthritis in Norway
- What are the differences in costs across the regional health authorities
- What are the differences in costs across patient`s sex
- What are the changes in costs from 2009 – 2012
- What is the prevalence of rheumatoid arthritis in Norway

Additionally we aim to explore the use of biologics among rheumatoid arthritis patients in Norway during the period 2009 - 2012.

3. Methods

We used a prevalence approach to this analysis limited to hospital costs and cost of pharmaceuticals. The analysis is based on observed data from the Norwegian Patient Registry and the Norwegian Prescription Database.

In accordance with the societal perspective of this analysis, all costs are presented without value added tax as this represents a transfer cost and not a cost to society. All costs are expressed in 2012 NOK and the present value of historic costs was calculated using actual inflation rates (Statistics Norway (SSB)).

Population data was extracted from Statistics Norway (Appendix 12, 13).

3.1 Data

3.1.1 The Norwegian Patient Registry

The Norwegian Patient Registry (NPR) contains information about all individuals who have received- or awaits specialized health care in Norway. NPR receives data from specialised health care institutions through standardized reports. The reports are based on registrations made by health care personnel. Thus, the system is vulnerable to human error. Even though most hospitals have established routines to detect errors in the patient data registration, it is unlikely that the information that is reported to NPR is perfect. Moreover, some variables in the patient data influence the hospitals income. Hence, health care personnel have an incentive to make registrations that are financially favourable.

Data on each episode of care in general hospitals (out-patient clinic visit, day care and in-patient care), consultations by specialists and treatment at private rehabilitation clinics were extracted from the Norwegian Patient Registry. We included only episodes with ICD-10 codes «M05 – Seropositive rheumatoid Arthritis» and «M06 – Other Rheumatoid Arthritis» as either main diagnosis or secondary diagnoses. Data were collected for the period 2009 – 2012. Variables that were included in the data set were:

- Gender
- Age (10 year intervals)
- Residence (Regional Health Authority)
- Year of care (2009 – 2012)
- DRG code
- DRG weight
- Biologic pharmaceuticals

Private rehabilitation clinics represented 0.7% of the episodes, consultations by specialists represented 10.0% and 89.3% of the episodes are treatment in general hospital. In total, 269,885 episodes were registered during the period. We counted the number of rheumatoid arthritis-surgical operations by defining DRG 209C, 209D, 209E, 209F, 209G, 209O, 218, 219, 220O, 220, 221, 222O, 222P, 222, 223O, 223, 224O, 224, 225O, 225, 226, 227O, 227, 228O, 228, 229O, 229, 233, 234O and 234 as rheumatic surgery.

The NPR is required to anonymise any released data material and, in that regard, information about DRG had been deleted in 19,768 of the episodes in our dataset.

We used estimates from the Norwegian DRG-system to estimate the cost of in-hospital care, out-hospital care and biologic pharmaceuticals administered in hospital. DRG is a system that aims to classify hospital episodes in homogenous groups based on resource-intensity and medical characteristics. All DRGs are assigned a cost-weight which expresses the mean cost of all episodes within a DRG relative to the average hospital episode. The average episode is given a weight of 1 along with a unit price. I will call this price the DRG unit price. The Norwegian DRG cost weights are computed based on patient- and accounting data from a representative sample of Norwegian hospitals. The system is revised annually to accommodate the changes in medical practice and development in medical technology. This entails that DRG weights and the DRG unit price vary from year to year. Norwegian hospitals are financed, in part, based on activity, and the DRG system is the foundation of this scheme (51-54). The Norwegian Health Directorate publishes rules for activity based

financing (51-54) annually. These publications include changes in DRG, updated DRG-weights and the updated DRG unit price.

2009 was a transition period in the funding of out-patient care. Before 2009, out-patient clinic care was not included in the activity based funding-scheme, but was financed through a fee for service. In 2009, out-patient care was included in the activity based funding-scheme, but the unit price for out-patient care and in-hospital care were different (51). This meant that for episodes in 2009 with missing information about DRG-code, which is the only variable that determine whether the episode is out-hospital care or in-hospital care, there was no way to determine whether to apply the out-patient unit price or the standard DRG unit price. In total, 54,250 in-hospital episodes were registered in 2009 of which 5,240 lacked information about DRG-code. By 2010, out-patient care was fully integrated in the DRG-system.

The DRG unit price (Appendix 15) served as our multiplier in the costing of hospital care. DRG-weight for each episode was multiplied with the unit price for the relevant year and the statistical software SPSS was used to aggregate estimates to patient level. By assuming that missing DRG values were out-patient care, the cost estimates for 2009 appeared to be greatly underestimated (Table 2). Assuming standard unit price yielded estimates that appeared to be more in line with the estimates for the following years. However, it is likely that this assumption results in an overestimation of the true cost since it is likely that at least some episodes are out-patient care.

TABLE 2 Total annual cost of hospital care (2012 NOK)

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|---------------|--------------------------|--------------------------|---------------------------|------------------------------------|---------|-------------|
| 2009** | 61 947 122 | 31 289 701 | 19 902 272 | 225 206 951 | 17 612 | 338 363 658 |
| 2009* | 123 700 156 | 74 699 752 | 49 288 775 | 337 998 125 | 580 358 | 586 267 166 |
| 2010 | 119 122 555 | 74 261 810 | 44 552 900 | 347 919 088 | 659 598 | 586 515 950 |
| 2011 | 119 388 173 | 81 058 851 | 45 615 273 | 364 193 702 | 537 231 | 610 793 229 |
| 2012 | 119 932 129 | 78 686 430 | 43 468 278 | 345 036 975 | 453 121 | 587 576 932 |

*Assumed that the episodes of care was out-patient care when the DRG-code was not stated

** Assumed that the episodes of care was in-hospital care when the DRG-code was not stated

The unit price for consultations by specialists were extracted from *fee schedule for private practice* (55). We assumed that consultation duration exceeded 20 minutes for all patients in this study which means a somewhat higher fee. In addition to the variable fee, the specialists receive an operating grant. The size of the grant depends on the specialist`s need for working space, technical equipment and auxiliary personnel. We assumed that on average rheumatic specialists receive a grant of NOK864,420, which represent the second of the three 2011/2012 operating grant classes⁴. We assumed that, on average, physicians have 2500 consultations per year. In total, this amounts to a unit price of NOK728.⁵

The unit price for treatment in private rehabilitation clinics is based on observed data from “Samdata 2012”. Samdata report only aggregated data, hence, this estimate yields a mean cost across all diagnosis combined and may differ from the true mean for rheumatoid arthritis-patients.

1. January 2006, the regional health authorities assumed responsibility for financing biologic pharmaceuticals. Initially, the regional health authorities` base funding were increased to compensate for the added costs and in 2009 self-administered biologic pharmaceuticals were included in the activity based funding scheme. The costs of self-administered biologic drugs were not, however, covered by the DRG weight, but

⁴ Class 1 = NOK744,120 Class 2 = NOK864,420 Class 3 = NOK1,108,140

⁵ Unit price of consultation by specialist: NOK307 + NOK75 + (NOK864,420 / 2500) = NOK727.768

financed based on the number of patients on a particular drug in a given year. Thus, the costs of these pharmaceuticals are not included in the data from the Norwegian Patient Registry, but registered in the Norwegian Prescription database. In 2010 the scheme was expanded to include biologic pharmaceuticals that were administered in out-patient clinics. Our analysis does not include costs of biologic pharmaceuticals administered in outpatient clinics during 2009.

3.1.2 The Norwegian Prescription Database

Data concerning pharmaceuticals that were not administered in hospital were extracted from the Norwegian Prescription Database at the Norwegian Institute of Public health. The Database contains data about all dispensed drugs in Norway. An online search engine was used to extract data on relevant pharmaceuticals. The search was built to include number of users, users per 1000 inhabitants, turnover in Norwegian crowns and turnover in doses for all relevant pharmaceuticals (Appendix 1).

The prescription registry does not have a diagnosis variable. It does however have a reimbursement code that can be used as a proxy for diagnosis for reimbursement drugs. This variable, however, is not available on the web-based search engine, but can be purchased on request. For financial reasons, this was not possible for this student study. Thus, we only could extract data on total sales for each pharmaceutical without any information on diagnosis. The thesis supervisor proposed estimates of the proportion of drugs attributable to rheumatoid arthritis.

3.2 Software

All data on analyses were performed in SPSS 20 or Excel 2010.

4. Results

In total, there were 269,885 specialised health care episodes with rheumatoid arthritis as the main- or secondary diagnosis during the period 2009 - 2012. There was a steady increase in the number of episodes during the period (Appendix 2). The majority of patients had seropositive rheumatoid arthritis (ICD 10 diagnosis M05) (Table 3).

TABLE 3 Number of episodes by ICD-10 diagnoses

| | Main diagnosis | Secondary diagnosis |
|--|----------------|---------------------|
| M05 - Seropositive Rheumatoid Arthritis | 173 272 | 26 266 |
| M06 - Other Rheumatoid Arthritis | 55 781 | 16 484 |

Source: Norwegian Patient Registry

Episodes with Rheumatoid arthritis as the secondary diagnosis accounted for approximately 50% of hospital costs⁶. Non-surgical cancer treatment (DRG 410A) was the most frequent DRG where rheumatoid arthritis was registered as a secondary diagnosis.

In total, 36,170 unique patients received specialised health care with rheumatoid arthritis as either main- or secondary diagnosis during the period 2009 – 2012. Among whom 71% of patients were women. The sex distribution was stable in time and across RHAs (Table 4). Women had on average more episodes than men representing 74% of episodes during 2009 - 2012. It is likely that all patients diagnosed with rheumatoid arthritis will receive specialised health care during the period of 4 years. On the basis of the 4-year period prevalence (n=36,170), the prevalence of RA as of January 1 2009 would be the period prevalence minus the incident cases during the period. The four year incidence was estimated at 25 per 100,000 per year equivalent to 100 per 100,000 during the four years. Assuming that all patients with RA had at

⁶ 2009: 69%, 2010: 54%, 2011: 47%, 2012: 47%

least one episode of care during the period, the point prevalence was 31,247 or 0.65% of the population.⁷

TABLE 4 Sex by year and regional health authority (RHA)

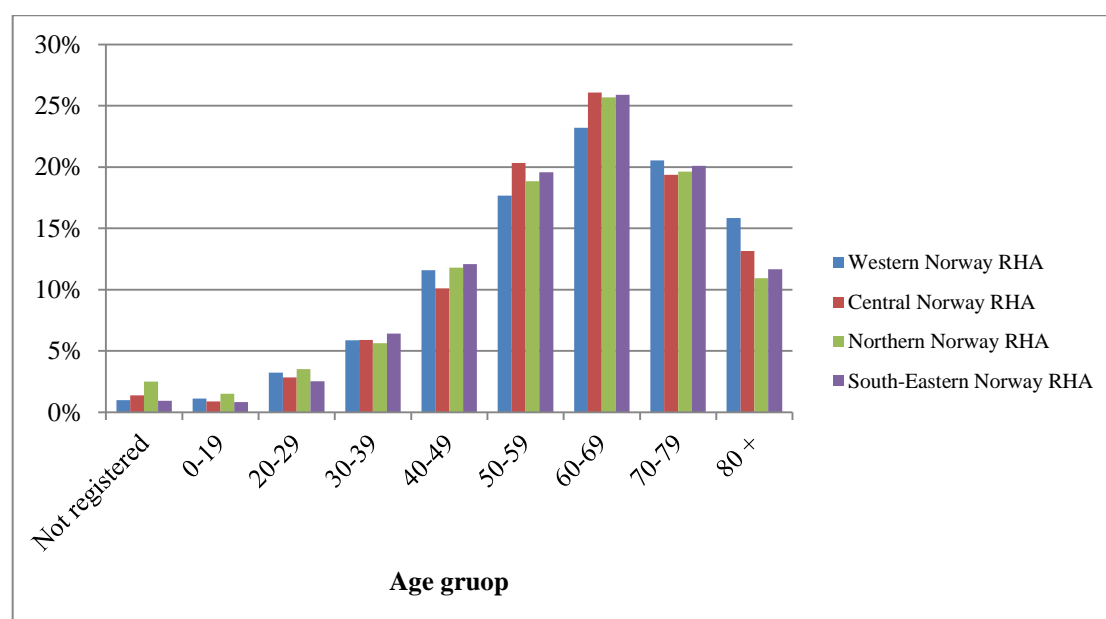
| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|---------------|--------------------------|--------------------------|---------------------------|------------------------------------|---------|---------|
| 2009 | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % |
| Female | 70.3 % | 70.8 % | 70.0 % | 71.6 % | 81.7 % | 71.1 % |
| 2010 | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % |
| Female | 70.4 % | 70.9 % | 70.7 % | 71.3 % | 66.7 % | 71.0 % |
| 2011 | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % |
| Female | 71.2 % | 72.0 % | 71.4 % | 71.2 % | 61.8 % | 71.3 % |
| 2012 | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % | 100.0 % |
| Female | 70.8 % | 71.3 % | 71.2 % | 71.3 % | 69.3 % | 71.2 % |

The mean age of patients was 62 years⁸ (females: 63, males: 62) and 65% of patients were in the age group 50 - 79 and 11% were less than 40 years old. The age distribution was similar across the Regional Health Authorities (Figure 4). Detailed tables on the age distribution are presented in appendix 3-5.

⁷ $36,170 - (4,922,409 / 100,000 * 100) = 31,247$. Assuming an incidence of 25 per 100,000 and that all new patients received specialised health care during the period. Population 1 January 2009: 4,779,252 (SSB) Average population during the period: 4,922,409. (Appendix 12,13)

⁸ Mean age was estimated based on age-group data (Appendix 10).

FIGURE 4 Age distribution of patients by regional health authority



4.1 Cost of hospital care

Approximately 97.0% of specialised somatic care costs were attributable to hospital care across time (2009 – 2012) and place (regional health authorities) (Appendix 6). Hospital care includes day care, in-patient care, out-patient care and treatment with biologic DMARDs administered in hospital (Costs for biologic DMARDs administered in outpatients clinics are only included for the period 2010-2012). The South Eastern Norway RHA account for most of the costs (57%) and The Northern Norway RHA account for the smallest part of the costs (8%). Hospital care costs amount to NOK12 million per 100,000 inhabitants nationally. From 2011 to 2012 the costs per capita dropped 5%. The South Eastern Norway RHA had the highest costs per capita (>NOK12 million per 100,000 inhabitants) and the Northern Norway RHA had the lowest (<NOK10 million per 100,000 inhabitants).

TABLE 5 Cost of hospital care by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|--------------|--------------------------|--------------------------|---------------------------|------------------------------------|---------|-------------|
| 2009* | 123 700 156 | 74 699 752 | 49 288 775 | 337 998 125 | 580 358 | 586 267 166 |
| 2010 | 119 122 555 | 74 261 810 | 44 552 900 | 347 919 088 | 659 598 | 586 515 950 |
| 2011 | 119 388 173 | 81 058 851 | 45 615 273 | 364 193 702 | 537 231 | 610 793 229 |
| 2012 | 119 932 129 | 78 686 430 | 43 468 278 | 345 036 975 | 453 121 | 587 576 932 |

*Assumed that the episodes of care was in-hospital care when the DRG-code was not stated

TABLE 6 Cost of hospital care per 100,000 inhabitants by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|--------------|-----------------------|-----------------------|------------------------|-----------------------------|------------|
| 2009* | 12 315 127 | 11 153 145 | 10 610 621 | 12 565 072 | 12 141 240 |
| 2010 | 11 677 131 | 10 973 511 | 9 541 543 | 12 765 595 | 11 996 026 |
| 2011 | 11 535 340 | 11 850 033 | 9 715 630 | 13 173 625 | 12 331 565 |
| 2012 | 11 417 323 | 11 366 190 | 9 196 521 | 12 308 737 | 11 708 049 |

*Assumed that the episodes of care was in-hospital care when the DRG-code was not stated

Cost per patient (Appendix 7)

4.2 Cost of private specialist care

Less than 1% of the total costs were attributable to consultations by specialists. The Western Norway RHA and the South-Eastern Norway HRA had the highest proportion ranging between 0.6% and 1.1% while the Central Norway RHA had the lowest (< 0.1%) (Appendix 6). The South Eastern Norway RHA and the Western Norway RHA had the highest costs per capita while the Central Norway RHA had the lowest (Table 8). On a national level and across all RHAs except the Northern Norway RHA, costs per capita dropped significantly from 2009 (NOK128,000) to 2010 (NOK77,000). During the remainder of the period there was an increase in costs.

TABLE 7 Cost of private specialist services by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|-------------|--------------------------|--------------------------|---------------------------|------------------------------------|---------|-----------|
| 2009 | 1 892 233 | 60 891 | 171 881 | 3 992 573 | 92 492 | 6 210 069 |
| 2010 | 924 014 | 34 726 | 210 621 | 2 519 147 | 91 345 | 3 779 853 |
| 2011 | 692 311 | 47 136 | 115 631 | 3 567 612 | 80 279 | 4 502 968 |
| 2012 | 1 050 169 | 45 122 | 95 338 | 4 373 886 | 140 459 | 5 704 973 |

TABLE 8 Cost of private specialist services per 100,000 inhabitants by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|-------------|-----------------------|-----------------------|------------------------|-----------------------------|---------|
| 2009 | 188 384 | 9 091 | 37 002 | 148 424 | 128 607 |
| 2010 | 90 578 | 5 131 | 45 107 | 92 431 | 77 309 |
| 2011 | 66 891 | 6 891 | 24 628 | 129 048 | 90 912 |
| 2012 | 99 974 | 6 518 | 20 170 | 156 033 | 113 677 |

Cost per patient (Appendix 8)

4.3 Cost of private rehabilitation clinics

Approximately 2% of costs were attributable to rehabilitation in private rehabilitation clinics. The Northern Norway RHA had the highest proportion (>3%) and the Western Norway RHA had the lowest proportion with close to 1% during the whole period (Appendix 6) (Table 9). The Northern Norway RHA also had the highest costs per capita (>NOK400,000). In comparison, the Western Norway RHA had less than half of this amount. The costs per capita of care in private rehabilitation clinics decreased during the period (Table 10). This trend was similar across all RHAs except for a small increase in the Western- and Central Norway RHA from 2010 to 2011.

TABLE 9 Cost of private rehabilitation clinics by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|-------------|--------------------------|--------------------------|---------------------------|------------------------------------|---------|------------|
| 2009 | 2 156 659 | 2 790 970 | 2 029 797 | 7 459 503 | 456 704 | 14 893 633 |
| 2010 | 1 242 530 | 1 814 094 | 2 162 002 | 6 610 259 | 0 | 11 828 884 |
| 2011 | 1 317 635 | 1 868 646 | 1 916 560 | 6 324 648 | 23 957 | 11 451 446 |
| 2012 | 1 173 893 | 1 676 990 | 1 964 474 | 5 198 669 | | 10 014 026 |

TABLE 10 Cost of private rehabilitation clinics per 100,000 inhabitants by year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|-------------|-----------------------|-----------------------|------------------------|-----------------------------|---------|
| 2009 | 214 709 | 416 710 | 436 964 | 277 307 | 308 438 |
| 2010 | 121 800 | 268 065 | 463 019 | 242 539 | 241 936 |
| 2011 | 127 310 | 273 178 | 408 210 | 228 775 | 231 198 |
| 2012 | 111 753 | 242 240 | 415 621 | 185 456 | 199 539 |

Cost per patient (Appendix 9)

4.4 Cost of self-administered pharmaceuticals

Costs of self-administered drugs increased from NOK351 million to NOK414 million during 2009 – 2012 (Table 11). Costs per capita varied considerably across regional health authorities (Table 13). The Northern Norway regional health authority had the highest costs per capita throughout the period with 44% to 69% higher costs than the other regions.

Table 11 Cost of self-administered pharmaceuticals by year. All costs in 2012NOK

| Pharmaceutical | 2009 | 2010 | 2011 | 2012 |
|---------------------------|--------------------|--------------------|--------------------|--------------------|
| Adalimumab | 127 954 886 | 161 992 386 | 151 914 913 | 163 712 090 |
| Anakinra | 0 | 612 652 | 503 514 | 1 610 808 |
| Azathioprine | 453 777 | 466 928 | 483 657 | 500 159 |
| Cerolizumab Pegol | 0 | 654 263 | 2 506 738 | 6 020 753 |
| Etanercept | 209 814 436 | 192 148 447 | 180 737 856 | 189 863 970 |
| Golimumab | 0 | 22 002 206 | 40 920 409 | 37 776 650 |
| Hydroxychloroquine | 1 254 545 | 1 335 243 | 1 362 710 | 1 374 330 |
| Leflunomid | 4 610 065 | 5 240 620 | 5 634 012 | 5 728 882 |
| Methotrexate | 1 848 501 | 2 304 759 | 2 718 700 | 3 171 889 |
| Sulfasalazine | 5 671 609 | 5 531 947 | 5 175 692 | 4 817 627 |
| Total | 351 607 819 | 392 289 453 | 391 958 200 | 414 577 157 |

Costs without value added tax

4.5 Total costs

Total costs increased from NOK958 million to NOK1.017 billion during the period (Table 12). Costs per capita increased marginally during the period (Table 13). Both total costs and costs per capita decreased from 2011 to 2012. Hospital care accounts for the largest proportion of costs (57.7% - 61.1%) and self-administered pharmaceuticals represent the second largest cost component (36.7% - 40.7%) (Appendix 6).

TABLE 12 Total costs by cost variable, year and region. All costs in 2012NOK

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South- Eastern Norway RHA | Other | Total |
|---|-----------------------|-----------------------|------------------------|------------------------------------|-----------|---------------|
| Cost of hospital care (including pharmaceuticals administered in hospital) | | | | | | |
| 2009 | 123 700 156 | 74 699 752 | 49 288 775 | 337 998 125 | 580 358 | 586 267 166 |
| 2010 | 119 122 555 | 74 261 810 | 44 552 900 | 347 919 088 | 659 598 | 586 515 950 |
| 2011 | 119 388 173 | 81 058 851 | 45 615 273 | 364 193 702 | 537 231 | 610 793 229 |
| 2012 | 119 932 129 | 78 686 430 | 43 468 278 | 345 036 975 | 453 121 | 587 576 932 |
| Cost of private specialist care | | | | | | |
| 2009 | 1 892 233 | 60 891 | 171 881 | 3 992 573 | 92 492 | 6 210 069 |
| 2010 | 924 014 | 34 726 | 210 621 | 2 519 147 | 91 345 | 3 779 853 |
| 2011 | 692 311 | 47 136 | 115 631 | 3 567 612 | 80 279 | 4 502 968 |
| 2012 | 1 050 169 | 45 122 | 95 338 | 4 373 886 | 140 459 | 5 704 973 |
| Cost of care in private rehabilitation clinics | | | | | | |
| 2009 | 2 156 659 | 2 790 970 | 2 029 797 | 7 459 503 | 456 704 | 14 893 633 |
| 2010 | 1 242 530 | 1 814 094 | 2 162 002 | 6 610 259 | 0 | 11 828 884 |
| 2011 | 1 317 635 | 1 868 646 | 1 916 560 | 6 324 648 | 23 957 | 11 451 446 |
| 2012 | 1 173 893 | 1 676 990 | 1 964 474 | 5 198 669 | | 10 014 026 |
| Cost of patient-administered pharmaceuticals | | | | | | |
| 2009 | 75 366 120 | 45 203 832 | 52 078 932 | 178 958 934 | | 351 607 819 |
| 2010 | 80 000 424 | 50 731 066 | 57 508 837 | 204 049 125 | | 392 289 453 |
| 2011 | 77 853 086 | 50 348 473 | 55 802 554 | 207 954 087 | | 391 958 200 |
| 2012 | 80 634 049 | 55 771 934 | 54 983 266 | 223 187 909 | | 414 577 157 |
| Total | | | | | | |
| 2009 | 203 115 168 | 122 755 446 | 103 569 385 | 528 409 135 | 1 129 554 | 958 978 688 |
| 2010 | 201 289 523 | 126 841 695 | 104 434 361 | 561 097 619 | 750 942 | 994 414 140 |
| 2011 | 199 251 205 | 133 323 106 | 103 450 017 | 582 040 048 | 641 466 | 1 018 705 843 |
| 2012 | 202 790 239 | 136 180 476 | 100 511 355 | 577 797 439 | 593 580 | 1 017 873 089 |

**TABLE 13 Total costs per 100,000 inhabitants by cost variable, year and region.
All costs in 2012NOK**

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|---|-----------------------|-----------------------|------------------------|-----------------------------|------------|
| Cost of hospital care (including pharmaceuticals administered in hospital) | | | | | |
| 2009 | 12 315 127 | 11 153 145 | 10 610 621 | 12 565 072 | 12 141 240 |
| 2010 | 11 677 131 | 10 973 511 | 9 541 543 | 12 765 595 | 11 996 026 |
| 2011 | 11 535 340 | 11 850 033 | 9 715 630 | 13 173 625 | 12 331 565 |
| 2012 | 11 417 323 | 11 366 190 | 9 196 521 | 12 308 737 | 11 708 049 |
| Cost of private specialist care | | | | | |
| 2009 | 188 384 | 9 091 | 37 002 | 148 424 | 128 607 |
| 2010 | 90 578 | 5 131 | 45 107 | 92 431 | 77 309 |
| 2011 | 66 891 | 6 891 | 24 628 | 129 048 | 90 912 |
| 2012 | 99 974 | 6 518 | 20 170 | 156 033 | 113 677 |
| Cost of care in private rehabilitation clinics | | | | | |
| 2009 | 214 709 | 416 710 | 436 964 | 277 307 | 308 438 |
| 2010 | 121 800 | 268 065 | 463 019 | 242 539 | 241 936 |
| 2011 | 127 310 | 273 178 | 408 210 | 228 775 | 231 198 |
| 2012 | 111 753 | 242 240 | 415 621 | 185 456 | 199 539 |
| Cost of patient-administered pharmaceuticals | | | | | |
| 2009 | 7 503 170 | 6 749 218 | 11 211 271 | 6 652 794 | 7 281 586 |
| 2010 | 7 842 137 | 7 496 423 | 12 316 214 | 7 486 823 | 8 023 507 |
| 2011 | 7 522 201 | 7 360 468 | 11 885 427 | 7 522 121 | 7 913 412 |
| 2012 | 7 676 216 | 8 056 210 | 11 632 731 | 7 961 933 | 8 260 858 |
| Total | | | | | |
| 2009 | 20 221 390 | 18 328 164 | 22 295 857 | 19 643 597 | 19 859 872 |
| 2010 | 19 731 646 | 18 743 130 | 22 365 883 | 20 587 388 | 20 338 779 |
| 2011 | 19 251 743 | 19 490 571 | 22 033 895 | 21 053 570 | 20 567 088 |
| 2012 | 19 305 266 | 19 671 158 | 21 265 044 | 20 612 158 | 20 282 124 |

4.6 Biologic pharmaceuticals

Costs of pharmaceuticals administered in hospital increased dramatically from 2010 to 2011 and decreased from 2011 to 2012 (Table 14). Cost estimates for 2009 are not included since infusion treatment in out-patient clinics was not a part of the activity based funding scheme and not included in our data.

TABLE 14 Costs of biologic pharmaceuticals administered in hospital (i.v.) by year and pharmaceutical. All costs in 2012NOK

| Pharmaceutical | 2010 | 2011 | 2012 |
|----------------|--------------------|--------------------|--------------------|
| Abatacept | 16 955 960 | 22 850 998 | 19 906 233 |
| Infliximab | 69 983 751 | 70 172 956 | 60 200 820 |
| Rituximab | 31 365 291 | 40 101 736 | 42 145 922 |
| Tocilizumab | 18 965 691 | 32 302 742 | 41 424 699 |
| Total | 137 270 692 | 165 428 432 | 163 677 674 |

Etanercept is the most common biologic pharmaceutical among rheumatoid arthritis-patients (Table 15). More than 3000 unique patients received Etanercept during 2010 – 2012 while only 55 patients received treatment with Anakinra. In total, the number of unique patients who received treatment with biologic pharmaceuticals increased from 3792 to 4323 during 2010 – 2012 (Table 16). More than 200 unique patients received treatment with at least two biologic pharmaceuticals in the same year during 2010 – 2012. The most frequent combinations were Infliximab – Rituximab, Infliximab – Tocilizumab and Adalimumab – Etanercept (Table 18) and this was consistent during the period. In total, 73 unique patients received treatment with 3 or more biologic pharmaceuticals during the same year. The most frequent drug-combination was Abatacept, Infliximab and Tocilizumab (Table 17).

TABLE 15 Number of unique patients on biologic DMARDs by type of biologic and year

| Pharmaceutical | Type of administration | 2010 | 2011 | 2012 | 2010 - 2012 |
|----------------|------------------------|------|------|------|-------------|
| Rituximab | i.v | 714 | 826 | 890 | 1233 |
| Abatacept | i.v | 172 | 159 | 149 | 260 |
| Etanercept | s.c | 1353 | 1724 | 1808 | 3011 |
| Infliximab | i.v | 903 | 735 | 674 | 1152 |
| Adalimumab | s.c | 725 | 566 | 512 | 1116 |
| Golimumab | s.c | 4 | 249 | 181 | 349 |
| Anakinra | s.c | 25 | 27 | 21 | 55 |
| Tocilizumab | i.v | 208 | 267 | 344 | 503 |

i.v=Intravenous, s.c=subcutaneous

TABLE 16 Number of unique patients on biologic DMARDs by period and the number of different drugs.

| Number of different drugs | 2009 | 2010 | 2011 | 2012 | 2009 - 2012 |
|---------------------------|------|------|------|------|-------------|
| 1 | 2801 | 3501 | 3937 | 4085 | 5419 |
| 2 | 173 | 270 | 268 | 221 | 1082 |
| 3 | 9 | 21 | 24 | 16 | 238 |
| 4 | 0 | 0 | 2 | 1 | 65 |
| 5 | 0 | 0 | 0 | 0 | 8 |
| 6 | 0 | 0 | 0 | 0 | 1 |
| 7 | 0 | 0 | 0 | 0 | 0 |
| 8 | 0 | 0 | 0 | 0 | 0 |

TABLE 17 Number of unique patients on three biologic pharmaceuticals in the same year by drug combination

| Combination of biologic pharmaceutical | Number of unique patients |
|--|---------------------------|
| Abatacept, Infliximab, Tocilizumab | 13 |
| Etanercept, Infliximab, Adalimumab | 8 |
| Rituximab, Etanercept, Infliximab | 7 |
| Rituximab, Infliximab, Tocilizumab | 6 |

TABLE 18 Number of unique patients who were on multiple biologic pharmaceuticals in the same year by year and drug combination.

| 2009 | Adminitrated | Rituximab | Abatacept | Etanercept | Infliximab | Adalimumab | Golimumab | Anakinra | Tocilizumab |
|-------------|--------------|-----------|-----------|------------|------------|------------|-----------|----------|-------------|
| Rituximab | i.v | | | | | | | | |
| Abatacept | i.v | 12 | | | | | | | |
| Etanercept | s.i | 12 | 5 | | | | | | |
| Infliximab | i.v | 36 | 22 | 12 | | | | | |
| Adalimumab | s.i | 8 | 3 | 35 | 22 | | | | |
| Golimumab | s.i | 0 | 0 | 0 | 0 | 0 | | | |
| Anakinra | s.i | 1 | 0 | 0 | 1 | 0 | 0 | | |
| Tocilizumab | i.v | 6 | 6 | 7 | 10 | 2 | 0 | 0 | |

| 2010 | Adminitrated | Rituximab | Abatacept | Etanercept | Infliximab | Adalimumab | Golimumab | Anakinra | Tocilizumab |
|-------------|--------------|-----------|-----------|------------|------------|------------|-----------|----------|-------------|
| Rituximab | i.v | | | | | | | | |
| Abatacept | i.v | 13 | | | | | | | |
| Etanercept | s.i | 19 | 2 | | | | | | |
| Infliximab | i.v | 40 | 28 | 26 | | | | | |
| Adalimumab | s.i | 14 | 9 | 48 | 17 | | | | |
| Golimumab | s.i | 0 | 0 | 0 | 0 | 0 | | | |
| Anakinra | s.i | 0 | 0 | 3 | 0 | 1 | 0 | | |
| Tocilizumab | i.v | 21 | 32 | 8 | 41 | 10 | 1 | 1 | |

| 2011 | Adminitrated | Rituximab | Abatacept | Etanercept | Infliximab | Adalimumab | Golimumab | Anakinra | Tocilizumab |
|-------------|--------------|-----------|-----------|------------|------------|------------|-----------|----------|-------------|
| Rituximab | i.v | | | | | | | | |
| Abatacept | i.v | 10 | | | | | | | |
| Etanercept | s.i | 28 | 6 | | | | | | |
| Infliximab | i.v | 25 | 17 | 34 | | | | | |
| Adalimumab | s.i | 10 | 3 | 46 | 12 | | | | |
| Golimumab | s.i | 8 | 2 | 22 | 7 | 5 | | | |
| Anakinra | s.i | 0 | 0 | 5 | 4 | 2 | 7 | | |
| Tocilizumab | i.v | 22 | 20 | 14 | 31 | 6 | 1 | 1 | |

| 2012 | Adminitrated | Rituximab | Abatacept | Etanercept | Infliximab | Adalimumab | Golimumab | Anakinra | Tocilizumab |
|-------------|--------------|-----------|-----------|------------|------------|------------|-----------|----------|-------------|
| Rituximab | i.v | | | | | | | | |
| Abatacept | i.v | 8 | | | | | | | |
| Etanercept | s.i | 22 | 4 | | | | | | |
| Infliximab | i.v | 23 | 13 | 21 | | | | | |
| Adalimumab | s.i | 8 | 0 | 37 | 2 | | | | |
| Golimumab | s.i | 3 | 2 | 17 | 3 | 5 | | | |
| Anakinra | s.i | 0 | 0 | 1 | 0 | 2 | 0 | | |
| Tocilizumab | i.v | 17 | 21 | 13 | 44 | 5 | 1 | 1 | |

In total, 6813 unique patients received treatment with biologic pharmaceuticals during the period 2009 – 2012. 5944 patients received only one biologic during the same year. 481 of these patients changed pharmaceutical from one year to the next (Table 19).

TABLE 19 Number of patients who changed between biologics from one year to the next by type of biologic pharmaceutical.

| | | Changed from | | | | | | | |
|------------|-------------|--------------|------------|----------|------------|-----------|------------|-----------|-------------|
| | | Abatacept | Adalimumab | Anakinra | Etanercept | Golimumab | Infliximab | Rituximab | Tocilizumab |
| Changed to | Abatacept | - | 5 | 0 | 7 | 1 | 2 | 12 | 4 |
| | Adalimumab | 2 | - | 0 | 43 | 0 | 4 | 2 | 0 |
| | Anakinra | 0 | 1 | - | 3 | 1 | 0 | 0 | 0 |
| | Etanercept | 5 | 56 | 2 | - | 5 | 21 | 5 | 5 |
| | Golimumab | 2 | 5 | 4 | 8 | - | 8 | 5 | 1 |
| | Infliximab | 2 | 3 | 0 | 14 | 0 | - | 3 | 1 |
| | Rituximab | 3 | 53 | 0 | 67 | 4 | 27 | - | 1 |
| | Tocilizumab | 6 | 15 | 1 | 30 | 4 | 6 | 22 | - |

4.7 Episodes of surgery

The number of surgical operations for inflammatory rheumatic joint disease registered with surgical DRGs (Appendix 11) decreased from 2009 to 2010 and increased during 2010 – 2012 (Table 20). From 2011 to 2012 the number of episodes in surgical DRGs increased by 27%.

TABLE 20 Number of episodes of surgery

| Year | Male | Female | Total |
|------|------|--------|-------|
| 2009 | 31 | 387 | 418 |
| 2010 | 28 | 340 | 368 |
| 2011 | 29 | 382 | 411 |
| 2012 | 26 | 496 | 522 |

4.8 Trends in type of care (In-hospital care, day care and out-patient care)

In-hospital care and day care had a negative trend during the period in terms of costs and the number of registered episodes while out-patient care had a positive trend

(Table 21-22, figure 4-5). The number of out-patient episodes increased from 37,000 to 47,000 from 2009 to 2010 and costs increased from NOK50 million to NOK143 million during the same period. The estimates in 2009, however, are likely to be lower than the true costs since out-patient administered biologic pharmaceuticals were not included in the activity based funding scheme in 2009 and thus are not included in our dataset.

TABLE 21 Hospital care costs by type (In-hospital, Out-hospital and Day care), year and RHA. All costs in 2012NOK

| | 2 009 | 2 010 | 2 011 | 2 012 |
|---------------------------------|-------------|-------------|-------------|-------------|
| Western Norway RHA | | | | |
| In-hospital care and day care | 49 629 884 | 35 919 081 | 31 620 505 | 33 955 956 |
| Out-patient care | 7 036 527 | 26 923 837 | 35 437 710 | 32 919 117 |
| Central Norway RHA | | | | |
| In-hospital care and day care | 22 174 270 | 16 598 609 | 16 626 913 | 14 217 378 |
| Out-patient care | 6 087 063 | 16 083 892 | 24 533 444 | 24 535 374 |
| Northern Norway RHA | | | | |
| In-hospital care and day care | 10 396 889 | 8 127 648 | 7 071 202 | 5 496 670 |
| Out-patient care | 7 526 694 | 12 477 962 | 16 872 417 | 17 257 515 |
| South-Eastern Norway RHA | | | | |
| In-hospital care and day care | 179 767 340 | 155 199 333 | 140 256 888 | 125 855 479 |
| Out-patient care | 29 542 871 | 87 683 541 | 128 702 687 | 123 724 983 |

FIGURE 5 Hospital care costs by type (In-hospital, Out-hospital and Day care) and Year

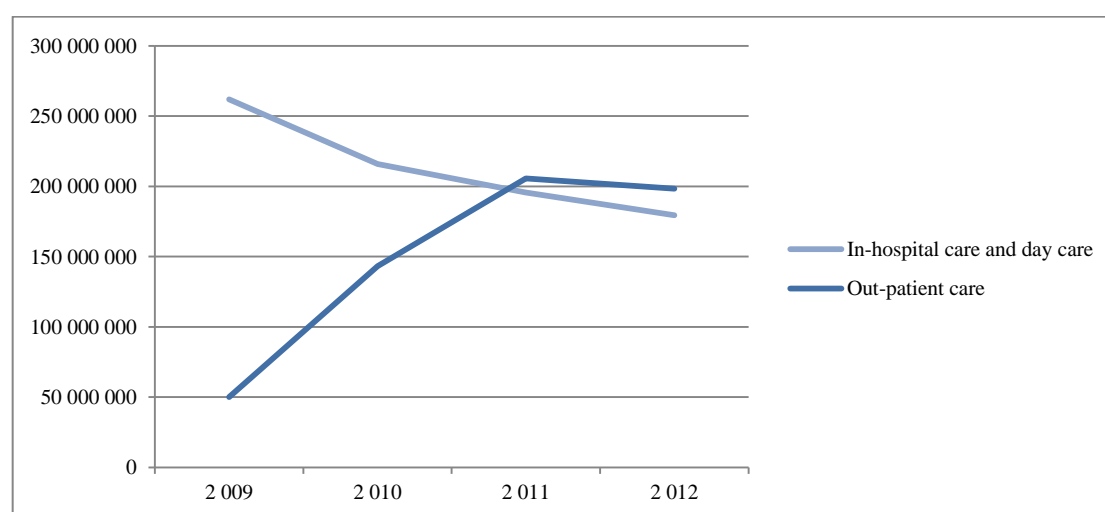
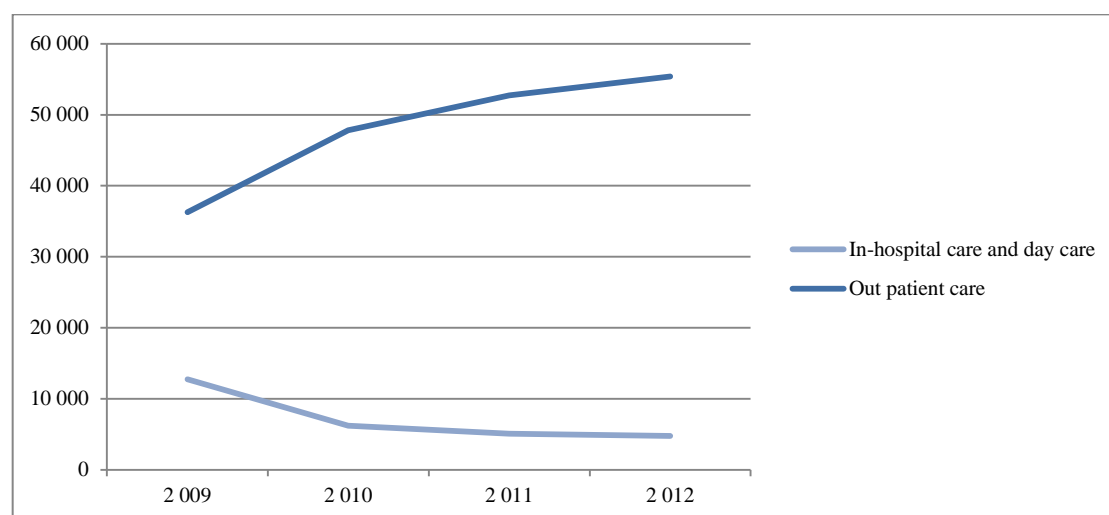


TABLE 22 Hospital episodes by type (In-hospital, Out-hospital and Day care), year and RHA

| | 2009 | 2010 | 2011 | 2012 |
|---------------------------------|--------|--------|--------|--------|
| Western Norway RHA | | | | |
| Out patient care | 4 870 | 6 935 | 7 128 | 7 762 |
| In-hospital care and day care | 2 750 | 1 305 | 1 112 | 1 176 |
| Central Norway RHA | | | | |
| Out patient care | 5 026 | 6 550 | 7 396 | 7 611 |
| In-hospital care and day care | 1 095 | 364 | 345 | 303 |
| Northern Norway RHA | | | | |
| Out patient care | 3 715 | 4 164 | 4 383 | 4 478 |
| In-hospital care and day care | 798 | 257 | 220 | 172 |
| South-Eastern Norway RHA | | | | |
| Out patient care | 22 666 | 30 185 | 33 832 | 35 553 |
| In-hospital care and day care | 8 090 | 4 305 | 3 393 | 3 110 |

FIGURE 6 Hospital episodes by type (In-hospital, Out-hospital and Day care), year and RHA



4.9 Distribution of hospital care costs

The median cost of hospital care per patient was NOK12,268 and the mean cost of hospital care per patient was NOK67,709. 12.5% of costs were attributable to the 1% most costly patients.

5. Discussion

The results of this study indicate that approximately 31,250 patients suffered from rheumatoid arthritis as of 1 January 2009. The disease poses a considerable financial burden on society with costs of more than NOK1 billion in 2012 for hospital care and pharmaceuticals. In 2012, hospital care costs, private specialist costs and costs of rehabilitation in private rehabilitation clinics amounted to NOK603 million or 0.5% of specialised health care expenditures⁹. Hospital care represents the largest cost component (57.7% - 61.1% of total costs). Self-administered pharmaceuticals represent the second largest cost component (36.7% - 40.7%) and increased from NOK351 million in 2009 to NOK414 million in 2012.

5.1 Strengths and limitations

An important strength of this study is the comprehensive data set that in principal captures all episodes of care for RA patients during four years. The validity of the variables age and sex is supposedly high. Unfortunately, the data set has several weaknesses that should be taken into consideration when interpreting the findings.

Husher and co-workers (42) define COI – analysis as an estimate of the maximum amount of money that could potentially be saved or gained if a disease were to be eliminated. In this regard, our study is limited in the sense that rheumatoid arthritis may cause other complications such as cardiovascular disease, respiratory diseases, cancer and infections. These conditions incur costs, but in treating these conditions rheumatoid arthritis might not always be registered as the main- or secondary diagnosis. Our study is also limited in that we only included cost of hospital care and pharmaceuticals. Previous studies indicate that indirect cost (production losses) account for a significant proportion of the total societal cost of rheumatoid arthritis (42, 45-48, 56-58). Moreover, primary care costs and direct non-medical costs are not included in our analysis. Additionally, some variables that are included in the analysis may be over- or underestimated. Out-patient administered biologic pharmaceuticals are not included for 2009 leading to an underestimation of hospital care costs.

⁹ Specialised health care expenditures in 2012 = NOK116 billion. (SSB)

Moreover, missing information about DRG lead to uncertain cost estimates for 2009 due to differences in DRG unit prices for out-patient care and in-hospital- and day care. The unit price for private specialist care is based on assumptions about rheumatologists' activity and operating grant which are uncertain and may lead to an over- or underestimation of the true costs. The costs of private rehabilitation care are based on aggregated data and are also uncertain.

Cost estimates include episodes of care with rheumatoid arthritis as either the main- or the secondary diagnosis and some episodes may not be caused in full by rheumatoid arthritis. This may lead to an overestimation of the costs that are attributable to rheumatoid arthritis.

An overarching limitation in our study is that the costs may not represent opportunity cost estimates. In economics, the true cost of a resource is its value in the best alternative project. Due to imperfections in the market for health care, no unit costs represent the opportunity costs.

The basis for estimating the unit cost for hospital care was the Norwegian DRG system. This system has two main possible sources of error. Firstly, the DRG weights and the unit price may not reflect the actual resource intensity of patient care. It would be utopic to think that the DRG system can keep up with the continuous and rapid development in medical technology. Thus, cost estimates based on this system are not likely to reflect actual costs perfectly. Moreover, heterogeneous resource intensity across patients within each DRG may also result in inaccurate estimates when the study sample is small. The DRG system, however, is constructed such that the average costs for large patient groups are correctly estimated. Even though the costs of the individual episode of care may be biased, the total costs are likely to be correct.

Secondly, the system relies on accurate registrations by health care personnel. In 2011, The Norwegian Directorate of Health performed a survey on DRG coding among health care personnel. In 14 of 21 health care enterprises, >40 % of health care personnel that were responsible for DRG-coding reported inadequate training. 2.2% reported knowledge about episodes of deliberate incorrect coding. Because

Norwegian hospitals have partly DRG financing, the choice of diagnosis has a direct relation to the hospitals' income. Hence, financial consequences may motivate the choice of diagnosis. As a result of this, the main- and secondary diagnoses that are reported to NPR may not reflect the true condition of the patients and thus yield biased data on rheumatoid arthritis-attributable health care consumption. In 2011, a revision by NPR¹⁰ of 4000 randomly selected in-patient care- and day care episodes revealed that 19.5% of episodes lacked consistency in main diagnosis-code reported to NPR and what was registered in the patient journal. In 4.2% of cases, the main diagnosis that was reported to NPR was registered as the secondary diagnosis in the patient journal. In 5.6% of the cases the main diagnosis that was reported to NPR was not registered as main- or secondary diagnosis in the patient journal.¹¹

Since the data on hospital episodes were not date-specific we were not able to reveal simultaneous use of multiple biologic pharmaceuticals. Patients who received more than one type of pharmaceutical during one year may have used them simultaneously or simply changed from one pharmaceutical to another.

We did not have access to diagnosis-specific data on consumption of patient-administered biologic pharmaceuticals. Data from the Norwegian Prescription Database were aggregated to yield total consumption independent of diagnosis. This meant that we had to use uncertain estimates of the proportion of drugs attributable to rheumatoid arthritis which in turn led to uncertainty in the cost estimates for patient-administered biologic pharmaceuticals.

5.2 Discussion of findings

Hospital care costs increased during the period 2009-2011 before decreasing in 2012. The lack of data on out-patient administered biologic pharmaceuticals may explain some of the difference between the 2009- and 2010 cost estimates. Despite an

¹⁰ <http://www.helsedirektoratet.no/kvalitet-planlegging/helsefaglige-kodeverk/kodeveiledning/Sider/nasjonal-gjennomgang-av-medisinsk-kodepraksis.aspx>

¹¹ http://www.helse-vest.no/aktuelt/rapporter/Documents/Internrevisjonsrapportar/HVIR_2011-Nasjonal-internrevisjon-av-medisinsk-kodepraksis-hovedrapport.pdf

increase in the number of patients and episodes of care, costs dropped from NOK610 million in 2011 to NOK587 million in 2012. One reason for this is that the DRG-weights for the most common DRGs in rheumatoid arthritis-treatment decreased (Table 23). If the adjustments of the DRG weights reflect an actual change in resource intensity of RA treatment, our estimates are correct and costs have in fact decreased. However, it could also be the case that our cost estimates for the period 2009-2011 are higher than the true cost or that the cost estimates for 2012 are lower than the true cost.

TABLE 23 Change in DRG-weight 2011 - 2012

| DRG | Frequency* | Percent** | Cumulative percent | Weight 2011 | Weight 2012 | Change 2011 - 2012 |
|------|------------|-----------|--------------------|-------------|-------------|--------------------|
| 908C | 90667 | 34 | 34 | 0,032 | 0,025 | -22 % |
| 908O | 29045 | 11 | 44 | 0,042 | 0,033 | -21 % |
| 808H | 25017 | 9 | 54 | 0,482 | 0,435 | -10 % |
| 908R | 20142 | 7 | 61 | 0,031 | 0,022 | -29 % |
| 808V | 13069 | 5 | 66 | 0,043 | 0,040 | -7 % |
| 410A | 6669 | 2 | 68 | 0,214 | 0,214 | 0 % |
| 242C | 5769 | 2 | 71 | 0,706 | 0,733 | 4 % |

* Number of episodes of care during 2009 - 2012

** Percent of total number of episodes of care during 2009 - 2012

Hospital care costs were more than 30% higher per capita in the South Eastern Norway RHA compared to the Northern Norway RHA during the period 2010 – 2012. The reasons for the regional differences in hospital care costs are not explored in this study, but deserve future research.

Costs of care in private rehabilitation clinics differed across regional health authorities. Demand for private rehabilitation services are likely to be influenced by supply and it is possible that some of the variation is due to differences in the number of private rehabilitation clinics across regions. Similarly, the differences in costs of private specialist care may be a result of differences in accessibility of specialists across regions.

Costs of self-administered pharmaceuticals increased during the period. Costs of biologic pharmaceuticals administered in hospital increased considerably from 2010 to 2011 but decreased from 2011 to 2012. The latter finding was an unexpected one as treatment with biologic pharmaceuticals has proven effective among rheumatoid arthritis patients. The majority of episodes related to hospital administered biologic pharmaceuticals are registered in DRG 808H. The weight for DRG 808H decreased by 10% from 2011 to 2012 which directly affects the cost estimate thus indicating that the reduction in costs does not necessarily mirror the trends in consumption. When we examined the number of patients who received biologic pharmaceuticals we found that treatment with biologics increased during 2009 - 2012.

The number of episodes registered with surgical DRGs also increased during the period and we found no indications of a trade-off between pharmaceuticals and surgery. We did find, however, that women had on average more surgery than men representing more than 90% of surgeries.

The number of out-patient care episodes increased dramatically in the period and the number of day care and in-hospital care episodes decreased. From 2009 to 2010 out-patient care episodes increased by 31%. This can be explained, at least in part, by the inclusion of out-patient administered biologic drugs in the activity based funding scheme in 2010.

Our study yields high hospital cost estimates compared what is reported by other studies (42, 46-49). As discussed in the literature review, there are methodological differences across the studies that may explain some of the variation. Different time periods may also explain some of the difference. The studies by Guillemin and co-workers, Husher and co-workers, Jacobsen and co-workers, and Westhovens and co-workers are based on data collected in the early 2000s. It is approximately 10 years between these studies and our study during which there has been considerable development in RA-treatment. Moreover, Norway is of the countries in the world with the highest health care costs. This may also contribute to the difference.

The findings of this study indicate that during 2009-2012 in total 36,170 unique patients received care in somatic hospitals with RA as the main or supplementary diagnosis. This number, however, also included those who did not have the disease on 1st of January 2009, but developed it during the subsequent four years. The incidence of RA in Norway has been estimated at 25 per 100,000 per year which means that 36,170 is an overestimate of the point prevalence (14). Subtracting 4,923 based on the four year cumulative incidence, the number is down to 31,247. Patients who did not have any episodes of care during the period, are not included which means that the latter number is somewhat underestimated, but this bias is likely very small. A prevalence of 31,247 means that prevalence proportion is 0.65% in Norway. This is in line with estimates reported by Symmons and co-workers on the prevalence of RA in The United Kingdom (59) and the overall prevalence of RA in developed countries (12). Our estimate is slightly higher, however, than that from a Norwegian study by Kvien and co-workers (13). Kvien and co-workers estimated the prevalence based on a patient register and a population survey of one county representing approximately 10% of the Norwegian population. They estimated the prevalence of RA among inhabitants between 20 and 79 years of age, whereas our estimate is based on all age groups. The differences in methodology may likely explain the difference between Kvien's and our estimate.

A number of cost studies of Rheumatoid Arthritis have been undertaken (42, 45-48, 56-58), but development in treatment technology, and pharmaceuticals means that it is important to update these studies continuously. Though this cost-of-illness study does not provide information about the health benefits behind the costs, it may provide important cost data for future cost effectiveness studies.

Future cost of illness-studies on rheumatoid arthritis will provide valuable knowledge about the continued development of cost over time. However, the scale of RA-costs and the scarcity of health care resources lead to the need for making the most of the resources at hand. Hence, the main focus of future research should be on identifying cost effective interventions through cost effectiveness analyses or cost utility analyses.

6. Conclusion

Afflicting more than 31,000 patients, rheumatoid arthritis poses a considerable burden on the Norwegian society in terms of hospital costs and costs of pharmaceuticals. In total, costs of pharmaceuticals and hospital care amounted to NOK1.018 billion in 2012. There was an increase in costs during the period 2009-2011 and a small decrease from 2011 to 2012. Total costs and costs per capita differed considerably across the regional health authorities. The use of biologic pharmaceuticals increased during the period. The data do not, however, indicate that the increased use of biologics has reduced the use of surgery for rheumatoid arthritis.

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APPENDIX

Appendix 1 Variables in the data extraction from the Norwegian Prescription Database

| |
|---|
| Measures |
| Number of users |
| Users per 1000 inhabitants |
| Turnover (NOK) |
| Turnover (Number of doses) |
| Pharmaceutical |
| L04AB05 Certolizumab pegol |
| L04AB06 Golimumab |
| L04AB01 Etanercept |
| L04AC03 Anakinra |
| L04AB04 Adalimumab |
| A07EC01 sulfasalazine |
| L01BA01 Methotrexate |
| L04AX03 Methotrexate |
| L04AA13 Leflunomide |
| P01BA02 Hydroxychloroquine |
| L04AX01 Azathioprine |
| Variables |
| Period (2009-2012) |
| Age (0 - 4, 5 - 9, 10 - 14, 15 - 19, 20 - 24, 25 - 29, 30 - 34, 35 - 39, 40 - 44, 45 - 49, 50 - 54, 55 - 59, 60 - 64, 65 - 69, 70 - 74, 75 - 79, 80 - 84, 85 - 89, 90+) |
| Sex |
| Regional Health Authority |

Appendix 2 Number of hospital episodes per year

| Year | Number of episodes |
|------|--------------------|
| 2009 | 62893 |
| 2010 | 64642 |
| 2011 | 69296 |
| 2012 | 73053 |

Appendix 3 Number of patients per age group

| | Frequency | Percent | Cumulative Percent |
|----------------|--------------|----------------|--------------------|
| Not registered | 413 | 1,1 % | 1,1 % |
| 0-19 | 345 | 1,0 % | 2,1 % |
| 20-29 | 992 | 2,7 % | 4,8 % |
| 30-39 | 2227 | 6,2 % | 11,0 % |
| 40-49 | 4222 | 11,7 % | 22,7 % |
| 50-59 | 6981 | 19,3 % | 42,0 % |
| 60-69 | 9191 | 25,4 % | 67,4 % |
| 70-79 | 7251 | 20,0 % | 87,4 % |
| 80 + | 4548 | 12,6 % | 100,0 % |
| Total | 36170 | 100,0 % | |

Based on patient's age at the time of the first registration

Appendix 4 Age distribution by regional health authority

| | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|----------------|--------------------|--------------------|---------------------|--------------------------|--------|--------|
| Not registered | 1,0 % | 1,4 % | 2,5 % | 0,9 % | 0,3 % | 1,1 % |
| 0-19 | 1,1 % | 0,9 % | 1,5 % | 0,8 % | 0,9 % | 1,0 % |
| 20-29 | 3,2 % | 2,8 % | 3,5 % | 2,5 % | 3,1 % | 2,8 % |
| 30-39 | 5,9 % | 5,9 % | 5,6 % | 6,4 % | 6,1 % | 6,2 % |
| 40-49 | 11,6 % | 10,1 % | 11,8 % | 12,1 % | 10,1 % | 11,7 % |
| 50-59 | 17,7 % | 20,3 % | 18,8 % | 19,6 % | 22,1 % | 19,3 % |
| 60-69 | 23,2 % | 26,1 % | 25,7 % | 25,9 % | 31,6 % | 25,4 % |
| 70-79 | 20,5 % | 19,4 % | 19,6 % | 20,1 % | 17,8 % | 20,0 % |
| 80 + | 15,8 % | 13,1 % | 10,9 % | 11,7 % | 8,0 % | 12,5 % |

Based on patient's age at the time of the first registration

Appendix 5 Sex distribution by age and regional health authority

| | Male | Female | Not registered | Total |
|---------------------------------|--------------|--------------|----------------|--------------|
| Western Norway RHA | | | | |
| Not registered | 11 (0,005) | 55 (0,012) | | 66 (0,01) |
| 0-19 | 31 (0,015) | 45 (0,009) | | 76 (0,011) |
| 20-29 | 53 (0,026) | 166 (0,035) | | 219 (0,032) |
| 30-39 | 117 (0,058) | 282 (0,059) | | 399 (0,059) |
| 40-49 | 233 (0,115) | 555 (0,116) | 1 (0,091) | 789 (0,116) |
| 50-59 | 375 (0,185) | 829 (0,174) | | 1204 (0,177) |
| 60-69 | 518 (0,255) | 1058 (0,222) | 5 (0,455) | 1581 (0,232) |
| 70-79 | 430 (0,212) | 966 (0,203) | 3 (0,273) | 1399 (0,205) |
| 80 + | 264 (0,13) | 812 (0,17) | 2 (0,182) | 1078 (0,158) |
| Total | 2032 (1) | 4768 (1) | 11 (1) | 6811 (1) |
| Central Norway RHA | | | | |
| Not registered | 13 (0,009) | 53 (0,016) | | 66 (0,014) |
| 0-19 | 11 (0,008) | 32 (0,009) | | 43 (0,009) |
| 20-29 | 31 (0,021) | 106 (0,031) | | 137 (0,028) |
| 30-39 | 79 (0,054) | 207 (0,061) | | 286 (0,059) |
| 40-49 | 155 (0,106) | 334 (0,099) | | 489 (0,101) |
| 50-59 | 298 (0,203) | 687 (0,203) | | 985 (0,203) |
| 60-69 | 418 (0,285) | 846 (0,25) | | 1264 (0,261) |
| 70-79 | 294 (0,201) | 645 (0,191) | | 939 (0,194) |
| 80 + | 166 (0,113) | 471 (0,139) | | 637 (0,131) |
| Total | 1465 (1) | 3381 (1) | | 4846 (1) |
| Northern Norway RHA | | | | |
| Not registered | 14 (0,013) | 76 (0,03) | | 90 (0,025) |
| 0-19 | 18 (0,016) | 36 (0,014) | | 54 (0,015) |
| 20-29 | 38 (0,034) | 89 (0,035) | | 127 (0,035) |
| 30-39 | 63 (0,057) | 141 (0,056) | | 204 (0,056) |
| 40-49 | 135 (0,122) | 292 (0,116) | | 427 (0,118) |
| 50-59 | 224 (0,202) | 458 (0,182) | | 682 (0,188) |
| 60-69 | 316 (0,285) | 614 (0,244) | | 930 (0,257) |
| 70-79 | 200 (0,181) | 510 (0,203) | | 710 (0,196) |
| 80 + | 100 (0,09) | 296 (0,118) | | 396 (0,109) |
| Total | 1108 (1) | 2512 (1) | | 3620 (1) |
| Other | | | | |
| Not registered | 1 (0,01) | | | 1 (0,003) |
| 0-19 | 2 (0,021) | 1 (0,004) | | 3 (0,009) |
| 20-29 | 4 (0,042) | 6 (0,026) | | 10 (0,031) |
| 30-39 | 5 (0,052) | 15 (0,066) | | 20 (0,061) |
| 40-49 | 10 (0,104) | 23 (0,1) | | 33 (0,101) |
| 50-59 | 19 (0,198) | 53 (0,231) | | 72 (0,221) |
| 60-69 | 37 (0,385) | 65 (0,284) | 1 (1) | 103 (0,316) |
| 70-79 | 15 (0,156) | 43 (0,188) | | 58 (0,178) |
| 80 + | 3 (0,031) | 23 (0,1) | | 26 (0,08) |
| Total | 96 (1) | 229 (1) | 1 (1) | 326 (1) |
| South-Eastern Norway RHA | | | | |
| Not registered | 31 (0,005) | 161 (0,011) | | 192 (0,009) |
| 0-19 | 71 (0,012) | 102 (0,007) | | 173 (0,008) |
| 20-29 | 118 (0,019) | 407 (0,028) | 1 (0,2) | 526 (0,025) |
| 30-39 | 349 (0,057) | 990 (0,067) | | 1339 (0,064) |
| 40-49 | 785 (0,128) | 1735 (0,118) | 1 (0,2) | 2521 (0,121) |
| 50-59 | 1274 (0,208) | 2808 (0,191) | | 4082 (0,196) |
| 60-69 | 1709 (0,279) | 3689 (0,25) | 1 (0,2) | 5399 (0,259) |
| 70-79 | 1192 (0,195) | 3001 (0,204) | 1 (0,2) | 4194 (0,201) |
| 80 + | 586 (0,096) | 1845 (0,125) | 1 (0,2) | 2432 (0,117) |
| Total | 6115 (1) | 14738 (1) | 5 (1) | 20858 (1) |

Proportions in the parenthesis

Based on patient's age at the time of the first registration

Appendix 6 Proportion of total costs by type of care and region

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|---|--------------------|--------------------|---------------------|--------------------------|--------|--------|
| Cost of hospital care (including pharmaceuticals administered in hospital) | | | | | | |
| 2009 | 60,9 % | 60,9 % | 47,6 % | 64,0 % | 51,4 % | 61,1 % |
| 2010 | 59,2 % | 58,5 % | 42,7 % | 62,0 % | 87,8 % | 59,0 % |
| 2011 | 59,9 % | 60,8 % | 44,1 % | 62,6 % | 83,8 % | 60,0 % |
| 2012 | 59,1 % | 57,8 % | 43,2 % | 59,7 % | 76,3 % | 57,7 % |
| Cost of private specialist care | | | | | | |
| 2009 | 0,9 % | 0,0 % | 0,2 % | 0,8 % | 8,2 % | 0,6 % |
| 2010 | 0,5 % | 0,0 % | 0,2 % | 0,4 % | 12,2 % | 0,4 % |
| 2011 | 0,3 % | 0,0 % | 0,1 % | 0,6 % | 12,5 % | 0,4 % |
| 2012 | 0,5 % | 0,0 % | 0,1 % | 0,8 % | 23,7 % | 0,6 % |
| Cost of care in private rehabilitation clinics | | | | | | |
| 2009 | 1,1 % | 2,3 % | 2,0 % | 1,4 % | 40,4 % | 1,6 % |
| 2010 | 0,6 % | 1,4 % | 2,1 % | 1,2 % | 0,0 % | 1,2 % |
| 2011 | 0,7 % | 1,4 % | 1,9 % | 1,1 % | 3,7 % | 1,1 % |
| 2012 | 0,6 % | 1,2 % | 2,0 % | 0,9 % | 0,0 % | 1,0 % |
| Cost of self-administered pharmaceuticals | | | | | | |
| 2009 | 37,1 % | 36,8 % | 50,3 % | 33,9 % | 0,0 % | 36,7 % |
| 2010 | 39,7 % | 40,0 % | 55,1 % | 36,4 % | 0,0 % | 39,4 % |
| 2011 | 39,1 % | 37,8 % | 53,9 % | 35,7 % | 0,0 % | 38,5 % |
| 2012 | 39,8 % | 41,0 % | 54,7 % | 38,6 % | 0,0 % | 40,7 % |

Appendix 7 Costs per patient of hospital care by year and region

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|------|--------------------|--------------------|---------------------|--------------------------|-------|--------|
| 2009 | 30 090 | 28 317 | 22 978 | 28 837 | 8 174 | 28 362 |
| 2010 | 29 596 | 27 073 | 20 703 | 29 980 | 6 467 | 28 470 |
| 2011 | 32 522 | 27 874 | 21 578 | 29 935 | 7 069 | 29 202 |
| 2012 | 29 804 | 26 107 | 19 607 | 26 656 | 5 149 | 26 406 |

Appendix 8 Costs per patient of private specialist services by year and region

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|------|--------------------|--------------------|---------------------|--------------------------|-------|-------|
| 2009 | 460 | 23 | 80 | 341 | 1 303 | 300 |
| 2010 | 230 | 13 | 98 | 217 | 896 | 183 |
| 2011 | 189 | 16 | 55 | 293 | 1 056 | 215 |
| 2012 | 261 | 15 | 43 | 338 | 1 596 | 256 |

Appendix 9 Costs per patient of private rehabilitation clinics

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|------|--------------------|--------------------|---------------------|--------------------------|-------|-------|
| 2009 | 525 | 1 058 | 946 | 636 | 6 432 | 721 |
| 2010 | 309 | 661 | 1 005 | 570 | 0 | 574 |
| 2011 | 359 | 643 | 907 | 520 | 315 | 547 |
| 2012 | 292 | 556 | 886 | 402 | 0 | 450 |

Appendix 9B Costs per patient of patient-administered DMARDs.

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|------|--------------------|--------------------|---------------------|--------------------------|--------|
| 2009 | 29 383 | 20 369 | 32 130 | 27 344 | 27 151 |
| 2010 | 29 796 | 22 058 | 34 509 | 29 591 | 28 958 |
| 2011 | 27 096 | 21 576 | 32 715 | 29 237 | 27 947 |
| 2012 | 26 381 | 23 317 | 32 571 | 30 267 | 28 571 |

Appendix 10 Age distribution of patients with at least one episode of care during the period 2009 - 2012

| Age group | Frequency | Percent | Cumulative Percent | From | To | Assumed mean per Age group | Tot patient years |
|--------------|--------------|---------|--------------------|------|-------------|----------------------------|-------------------|
| 0-19 | 345 | 1,0 % | 2,1 % | 0 | 19 | 11,5 | 3967,5 |
| 20-29 | 992 | 2,7 % | 4,8 % | 20 | 29 | 26,5 | 26288 |
| 30-39 | 2227 | 6,2 % | 11,0 % | 30 | 39 | 36,5 | 81285,5 |
| 40-49 | 4222 | 11,7 % | 22,7 % | 40 | 49 | 46,5 | 196323 |
| 50-59 | 6981 | 19,3 % | 42,0 % | 50 | 59 | 56,5 | 394426,5 |
| 60-69 | 9191 | 25,4 % | 67,4 % | 60 | 69 | 65 | 597415 |
| 70-79 | 7251 | 20,0 % | 87,4 % | 70 | 79 | 73,5 | 532948,5 |
| 80 + | 4548 | 12,6 % | 100,0 % | 80 | 99 | 88,5 | 402498 |
| Total | 35757 | | | | Mean | 62,50949 | |

Appendix 11 Surgical DRGs relevant for patients with rheumatoid arthritis

| DRG-Code | DRG-Text |
|----------|---|
| 209C | Major joint secondary procedure on hip |
| 209D | Major joint primary procedure on hip w cc |
| 209E | Major joint primary procedure on hip w/o cc |
| 209F | Major joint secondary procedure on knee/ankle |
| 209G | Major joint primary procedure on knee/ankle |
| 209O | Store leddingrep på underekstremitet, ikke reoperasjon, dagkirurgisk behandling |
| 218 | Op på humerus & kne/legg/fot ekskl kneleddsop > 17 år m/bk |
| 219 | Op på humerus & kne/legg/fot ekskl kneleddsop > 17 år u/bk |
| 220O | Op på humerus & kne/legg/fot, dagkirurgisk behandling |
| 220 | Op på humerus & kne/legg/fot ekskl kneleddsop 0-17 år |
| 221 | Operasjoner på kneledd ekskl proteseop m/bk |
| 222O | Other knee procedures, short therapy |
| 222P | Major knee procedures, short therapy |
| 222 | Operasjoner på kneledd ekskl proteseop u/bk |
| 223O | Større op på humerus/albue/underarm, dagkirurgisk behandling |
| 223 | Op på humerus/albue/underarm ekskl skulderprotese m/bk |
| 224O | Op på humerus/albue/underarm ekskl skulderprotese, dagkirurgisk behandling |
| 224 | Op på humerus/albue/underarm ekskl skulderprotese u/bk |
| 225O | Operasjoner på ankel og fot, dagkirurgisk behandling |
| 225 | Operasjoner på ankel & fot |
| 226 | Bløtdelsoperasjoner ITAD m/bk |
| 227O | Bløtdelsoperasjoner ITAD, dagkirurgisk behandling |
| 227 | Bløtdelsoperasjoner ITAD u/bk |
| 228O | Større op på håndlegg/hånd/tommel, dagkirurgisk behandling |
| 228 | Op på håndledd/hånd/tommel m/bk eller leddprotese håndledd/hånd |
| 229O | Op på håndledd/ hånd ekskl større leddop, dagkirurgisk behandling |
| 229 | Op på håndledd/hånd u/bk eller sårrevisjon på overekstremitet |
| 233 | Op på skjelett-muskelsystem og bindevev ITAD m/bk |
| 234O | Op på skjelett-muskelsystem og bindevev ITAD, dagkirurgisk behandling |
| 234 | Op på skjelett-muskelsystem og bindevev ITAD u/bk |

Appendix 12 Population of Norway

| Region | 1. January 2009 | 1. January 2010 | 1. January 2011 | 1. January 2012 | 1. January 2013 |
|---------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| South-Eastern Norway RHA | 2 672 951 | 2 707 012 | 2 743 875 | 2 785 259 | 2 821 116 |
| Østfold | 268 584 | 271 662 | 274 827 | 278 352 | 282 000 |
| Akershus | 527 625 | 536 499 | 545 653 | 556 254 | 566 399 |
| Oslo | 575 475 | 586 860 | 599 230 | 613 285 | 623 966 |
| Hedmark | 190 071 | 190 709 | 191 622 | 192 791 | 193 719 |
| Oppland | 184 288 | 185 216 | 186 087 | 187 147 | 187 254 |
| Buskerud | 254 634 | 257 673 | 261 110 | 265 164 | 269 003 |
| Vestfold | 229 134 | 231 286 | 233 705 | 236 424 | 238 748 |
| Telemark | 167 548 | 168 231 | 169 185 | 170 023 | 170 902 |
| Aust-Agder | 107 359 | 108 499 | 110 048 | 111 495 | 112 772 |
| Vest-Agder | 168 233 | 170 377 | 172 408 | 174 324 | 176 353 |
| Western Norway RHA | 996 712 | 1 012 202 | 1 028 069 | 1 041 886 | 1 058 994 |
| Rogaland | 420 574 | 427 947 | 436 087 | 443 115 | 452 159 |
| Hordaland | 469 681 | 477 175 | 484 240 | 490 570 | 498 135 |
| Sogn og Fjordane | 106 457 | 107 080 | 107 742 | 108 201 | 108 700 |
| Central Norway RHA | 666 164 | 673 364 | 680 110 | 687 968 | 696 602 |
| Møre og Romsdal | 248 727 | 251 262 | 253 904 | 256 628 | 259 404 |
| Sør-Trøndelag | 286 729 | 290 547 | 294 066 | 297 950 | 302 755 |
| Nord-Trøndelag | 130 708 | 131 555 | 132 140 | 133 390 | 134 443 |
| Northern Norway RHA | 463 425 | 465 621 | 468 251 | 470 757 | 474 563 |
| Nordland | 235 380 | 236 271 | 237 280 | 238 320 | 239 611 |
| Troms | 155 553 | 156 494 | 157 554 | 158 650 | 160 418 |
| Finnmark | 72 492 | 72 856 | 73 417 | 73 787 | 74 534 |
| Norway | 4 799 252 | 4 858 199 | 4 920 305 | 4 985 870 | 5 051 275 |

Source: SSB

Appendix 13 Population base for estimating costs per capita

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Total |
|-------------|-----------------------|-----------------------|------------------------|-----------------------------|-----------|
| 2009 | 1 004 457 | 669 764 | 464 523 | 2 689 982 | 4 828 726 |
| 2010 | 1 020 136 | 676 737 | 466 936 | 2 725 444 | 4 889 252 |
| 2011 | 1 034 978 | 684 039 | 469 504 | 2 764 567 | 4 953 088 |
| 2012 | 1 050 440 | 692 285 | 472 660 | 2 803 188 | 5 018 573 |

Source: SSB

Method: Population 2009 = (population per 1. January 2009 + population per 1. January 2010) / 2

Appendix 14 Number of patients per year and region

| Year | Western Norway RHA | Central Norway RHA | Northern Norway RHA | South-Eastern Norway RHA | Other | Total |
|-------|--------------------|--------------------|---------------------|--------------------------|-------|--------|
| 2009 | 4 111 | 2 638 | 2 145 | 11 721 | 71 | 20 671 |
| 2010 | 4 025 | 2 743 | 2 152 | 11 605 | 102 | 20 601 |
| 2011 | 3 671 | 2 908 | 2 114 | 12 166 | 76 | 20 916 |
| 2012 | 4 024 | 3 014 | 2 217 | 12 944 | 88 | 22 252 |
| Total | | | | | | 36 170 |

Appendix 15 DRG unit price by year and type (Day care, in-hospital care and out-patient care)

| Year | In-hospital care and day care | Out-hospital care |
|------|-------------------------------|-------------------|
| 2009 | 35 127 | 1 066 |
| 2010 | 35 964 | 35 964 |
| 2011 | 36 968 | 36 968 |
| 2012 | 38 209 | 38 209 |

Source: (51-54)